REMARKS

The claims have been amended to clarify the invention. Claims 1, 2 and 4 have been amended to recite the complete complement of recited sequences, and claim 8 has been amended to recite the further limitation that nucleic acids of the sample specifically hybridize with the complete complement of the cDNA encoding SEQ ID NO:1. Claim 2 has been further amended to delete recitation of fragments of SEQ ID NO:2 consisting of SEQ ID NO:4 and 5, which have now been incorporated into independent claim 3 in "consisting of " language. No new matter is added by any of these amendments, and entry of the amendments is requested. Claims 1-13 are under consideration.

Rejections Withdrawn

The Examiner has withdrawn the rejection of claim 6 under 35 U.S.C. § 112, first paragraph, as directed to non-statutory subject matter is withdrawn in view of applicants amendment.

35 U.S.C. § 112, Second Paragraph, Rejection of Claim 11

The Examiner has maintained the rejection of claim 11 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner reiterated that the method is vague and indefinite in that there is no definition or limitation for "a standard"; and there is no active method step linking the outcome of comparison with said standard to the diagnosis of colon cancer or colon polyps. The Examiner stated that applicants reference to the specification, in particular, page 18 of the specification reciting that "standard values can be obtained by using values obtained from normal subjects" does not provide a definition, or the metes and bounds, for a "standard value" but suggested how one can be obtained after experimentation

Applicants' Response

Applicants disagree that the use of the term "a standard" is not sufficiently set forth in the specification such that on skilled in the art could not determine the metes and bounds of the term in the ckaimed method. The Examiners' continued insistence that applicant provide a specific value for "a standard" in any and all experiments using the claimed method is clearly beyond the requirements of 35 U.S.C. § 112, second paragraph. The specification provides specific examples of such standards used in the claimed method at page 35, Example XI which describes

the preparation of matched normal and cancerous colon or colon polyp tissue samples from individual patients used in the study presented in Table 3. Table 3 presents a description of both the diseased sample (Cy5) and the microscopically normal, i.e., normal "standard" (Cy3), together with the differential expression ratio between the two samples (Cy5/Cy3), as described in the specification at page 6, lines 15-21. Thus, clearly the claimed method is sufficiently described, together with results of an exemplary experiment that the skilled artisan could similarly use the claimed method to achieve the same result with additional samples. Withdrawal of the rejection of claim 11 under 35 U.S.C. § 112, second paragraph is therefore requested.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 2, 8-10, 12 and 13

The Examiner has maintained the rejection of claims 2, 8-10, 12 and 13 under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a way as to reasonably to convey to one skill in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner stated, however, that the rejection of claims 7 and 11 is withdrawn in light of applicants amendments.

(A) As drawn to polynucleotides comprising ESTs

Claim 2 is drawn to an isolated DNA comprising SEQ ID NO:3-5 or the complement of SEQ ID NO:3-5 that are fragments of SEQ ID NO:2. The Examiner stated that, therefore, the claim is drawn to a genus of nucleic acids in that it encompasses any nucleic sequence that minimally comprises SEQ ID NO:3-5 within it. The specification does not address whether such partial cDNA sequences cross exon/intron splice junctions which would exclude the possibility of the claims reading on a full length gene. The Examiner stated that amendment of the product claims drawn to SEQ ID NO:3-5 to nucleic acids consisting of, rather than comprising, would obviate this part of the rejection.

Applicants Response

SEQ ID NO:3 was previously deleted in the response filed 6/11/2003, and SEQ ID NO:4 and 5 have been incorporated into independent claim 3 in consisting of language as the Examiner suggested.

(B) As drawn to a method of using a cDNA to detect expression of a nucleic acid, wherein said nucleic acid is not the complementary sequence of SEQ ID NO:2

Claim 8 is drawn to a method for using a cDNA to detect expression of a nucleic acid in a sample comprising hybridizing the composition of claim 4 to nucleic acid in a sample. Claim 4 encompasses both the cDNA of claim 1 and the complement of the isolated nucleic acid of claim 1. Thus, the Examiner stated, claim 8 is drawn in part to a method of using the nucleic acid encoding SEQ ID NO:1. Claims 8-13 depend upon a genus of expressed nucleic acids encompassing nucleic acids which encode intelectin and nucleic acids which encode a completely unrelated protein, as nucleic acids which hybridize to SEQ ID NO:2 would translate in the reverse of SEQ ID NO:2 and therefore would not encode intelectin or a protein related to intelectin. The specification teaches a method of using the complementary nucleic acid to the nucleic acids encoding SEQ ID NO:1 for the detection of nucleic acids encoding intelectin within a sample. However, since the claims depend upon a protein yet to be discovered, i.e., the translated protein product of the complement of the polynucleotide encoding SEQ ID NO:1, the disclosure of SEQ ID NO:2 is insufficient to describe the genus.

Applicants Response

Applicants stand corrected on the issue of the existence of mRNA as being primarily single stranded. Accordingly, claim 11 has been amended to reflect the fact, as the Examiner has stated, only the complement of a nucleic acid encoding SEQ ID NO:1, i.e., SEQ ID NO:2, would likely be useful in detecting differential expression of the mRNA of SEQ ID NO:2 in colon cancer or colon polyps versus normal colon. However, applicants disagree that the specification does not sufficiently describe the more generic method of using either SEQ ID NO:2 or any other degenerate nucleic acid sequence encoding SEQ ID NO:1, to detect its complete complement in a hybridization assay, or vice versa. Applicants "possession" of the claimed method does not require that it be used to detect a polynucleotide encoding a particular protein or a polynucleotide expressed in a particular condition. Applicants have established a utility for both the claimed polynucleotide and its complete complement based on the former encoding a useful protein, intelectin, as well as being differentially expressed in colon cancer or colon polyps, and the latter as useful for detecting the former, or vice versa, for whatever reasons the skilled artisan may choose. For example, a cDNA library constructed as described in Examples I and II of the specification, at page 25 would comprise various cDNAs representing expressed mRNAs. Therefore the skilled artisan may use either the cDNA of SEQ ID NO:2 or its complete

complement in the hybridization method described in claim 8 to determine whether the double stranded cDNA representing an mRNA of SEQ ID NO:2 is present in the tissue library. Applicants is not required to teach each and every use of a polynucleotide and its complete complement to satisfy the written description requirement according to 35 U.S.C. § 112, first paragraph.

(C) As drawn to a method of using a cDNA to screen a plurality of molecules which specifically bind the cDNA

Claim 12 is drawn to a method of using cDNA to screen a plurality of molecules or compounds comprising combining the cDNA of claim 1 with a plurality of molecules under conditions to allow for specific binding. Claim 13 embodies specific molecules or compounds to be screened. The Examiner stated that the specification describes a method of detecting colon cancer or colon polyps wherein hybridization of a nucleic acid probes which binds to SEQ ID NO:1 (sic, the nucleic acid encoding SEQ ID NO:1) is indicative of colon cancer or colon polyps. The Examiner stated, however, that the specification does not describe any active method steps in which detection of a nucleic acid probe to the complement of SEQ ID NO:2 is indicative of colon cancer or colon polyps. The Examiner stated that applicant has not provided a representative number of species of method steps for the detection of the complement of SEQ ID NO:2, nor are there a representative number of species of method steps for the detection of disease or pathological conditions beyond those of colon cancer or colon polyps.

Further, the Examiner stated, the specification has not described any method steps wherein specific peptides or transcription factors are identified by binding to SEQ ID NO:2 or the complement of SEQ ID NO:2. The Examiner then cited various examples in the art in support of an allegation that, general knowledge and skill in the art do not supplement the omitted description because there is no nexus between protein sequences which bind to DNA and transcription factor and the primary DNA sequence given by the nucleic acids which encode SEQ ID NO:1. See pages 6-7 of the Office Action and references therein.

Applicants Response

The Examiner appears to require that the method of claims 12 and 13 for identifying molecules or compounds that bind to either the cDNA encoding SEQ ID NO:1 or its complement either be connected with the detection of colon cancer and colon polyps as described in claim 11,

or that the specific molecules or compounds and their mechanisms of interaction with the claimed polynucleotides be known in order for their to be an adequate written description of the claimed method to satisfy the written description requirements of 35 U.S.C. § 112, first paragraph.

Applicants disagree. There is, first of all, no connection made, or required between the use of the claimed polynucleotides as recited in claim 1, in the hybridization method of claim 11 to detect differential expression associated with colon cancer or colon polyps, and the method of screening for molecules or compounds that specifically bind the claimed polynucleotides, as recited in claims 12 and 13. Nor does an adequate description of the claimed method require a disclosure of the specific molecules or compounds and their specific mechanisms of interaction with the claimed polynucleotides.

The specification describes "specific binding" as it relates to both polynucleotides and polypeptides of the invention at page 9, lines 12-15. "Ligands" are further described in the specification at page 8, lines 15-18 as "any agent, molecule or compound which will specifically bind to a polynucleotide or an epitope of a protein". The specification then describes methods of screening for and purifying various molecules, compounds or ligands that specifically bind a polynucleotide or protein at page 20, lines 12-31, which includes reference to specific assays to measure such binding, e.g., gel-retardation assay or a reticulocyte lysate transcriptional assay (lines 19-21). The specification further describes methods of screening in Example XV at pages 36-37 of the specification.

Thus, the specification adequately describes the claimed screening method as recited in claims 12 and 13 in terms that do not require a knowledge of the specific molecule or compound tested or its specific mechanism of interaction with the claimed polynucleotides. The methods disclosed, and referenced in the specification, are sufficiently well known in the art that their application to the specific polynucleotides and proteins of the instant application does not require the presentation of actual results of binding or purification assays to establish applicants "possession" of the claimed method.

With the above amendments and remarks, applicants submit that the claimed polynucleotides and their methods of use, at least as described in claims 2, 8-10, 12 and 13, are adequately described in the specification that one skilled in the art would recognize applicants

possession of them. Withdrawal of the rejection of these claims under 35 U.S.C. § 112, first paragraph, is therefore requested.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 4 and 8-11

The Examiner has rejected claims 4 and 8-11 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method of detecting colon cancer or colon polyps comprising detecting SEQ ID NO:2 or the nucleic acids encoding SEQ ID NO:1, does not reasonably provide enablement for a method of detecting colon cancer or colon polyps comprising detecting the complement of SEQ ID NO:2 or of the nucleic acids encoding SEQ ID NO:1.

The Examiner stated that, for the reasons stated above, sequence(s) which are complementary to SEQ ID NO:2 or the nucleic acids encoding SEQ ID NO:1 would not be expected to encode intelectin or a protein similar to intelectin. Furthermore, the Examiner stated, it would not be known to one of skill in the art how to use the hybridization complex recited in claim 8, as said hybridization complex would not be expected to be indicative of colon cancer or colon polyps, or any other disease or condition. The Examiner further stated that claims 8-10 are not limited to detection of colon cancer or colon polyps, and therefore read on a sample of DNA obtained from any organ or tissue, and additionally genomic DNA.

Applicants Response

Applicants disagree that the specification is not enabling for any use of the polynucleotide encoding SEQ ID NO:1 in a composition comprising the polynucleotide and a labeling moiety (claim 4), or in a hybridization assay to detect the presence of its complete complement (claims 8-10).

Applicants remarks in response to the rejection of these claims under 35 U.S.C. § 112, first paragraph, ¶ (B), above, are referenced herein. As noted above, claim 11 has been amended to reflect the use of only the complement of the polynucleotide encoding SEQ ID NO:1, specifically for the detection and diagnosis of colon cancer or colon polyps. However, for the reasons discussed above, the use of the claimed polynucleotides in a hybridization assay is not limited to only the detection or diagnosis of colon cancer or colon polyps. Having established the usefulness of a cDNA encoding SEQ ID NO:1 and its complete complement, the use of either sequence in a hybridization assay to detect either strand of the claimed cDNA is enabled for

whatever reason the skilled artisan may choose. An example of detecting the claimed cDNA in a cDNA library using either strand was given as an exemplary use. Additionally, since the claimed polynucleotides are recited specifically as "an isolated cDNA" they cannot read on any naturally occurring polynucleotide, such as genomic DNA. Withdrawal of the rejection of claims 4 and 8-11 under 35 U.S.C. § 112, first paragraph for lack of enablement is therefore requested.

35 U.S.C. § 112, First Paragraph, Rejection of Claims 12 and 13

The Examiner has rejected claims 12 and 13 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method of screening for colon cancer or colon polyps comprising the detection of nucleic acids which bind to the complement of SEQ ID NO:2 or the complement of nucleic acids encoding SEQ ID NO:1 in a sample of colon tissue, does not reasonably provide enablement for a method of screening for any other disease or condition comprising the detection of nucleic acids which bind to SEQ ID NO:2, the complement of SEQ ID NO:2, the complement of SEQ ID NO:2, the nucleic acids encoding SEQ ID NO:1, or the complement thereof, or a composition comprising the nucleic acids encoding SEQ ID NO:1 and a labeling moiety.

The Examiner stated that claims 12 is drawn to a method of screening a plurality of molecules or compounds, and claims 13 recites various categories of molecules or compounds to be screened. The Examiner stated that the specification teaches only the binding of nucleic acid sequence to nucleic acids encoding SEQ ID NO:1 or to SEQ ID NO:2, wherein detection of a hybridization complex is indicative of colon cancer or colon polyps. The species of DNA molecules, RNA molecules, peptide nucleic acids and artificial chromosomal constructs are commensurate in scope with the teachings of the specification regarding the detection of nucleic acids encoding SEQ ID NO:1 and colon cancer or colon polyps. However, the Examiner stated, the specification provides no teachings of how to use the broadly claimed molecules which bind to the complement of nucleic acids encoding SEQ ID NO:1, nor how to use peptides and transcription factors which bind to a nucleic acid of claim 1. The Examiner then reiterated arguments presented previously in the rejection of these claims under 35 U.S.C. 112, first paragraph, regarding an alleged lack of written description. The Examiner further stated that there is no enablement for the broadly claimed method beyond screening of molecules which hybridize to the nucleic acids which encode SEQ ID NO:1, wherein it is determined that the

nucleic acids are indicative of colon cancer or colon polyps.

Applicants Response

Applicants disagree that a method for screening molecules or compounds that specifically bind to either the polynucleotide encoding SEQ ID NO:1 or its complete complement is not enabled by the specification. Applicants again reference the remarks made in response to the rejection of these claims under 35 U.S.C. § 112, first paragraph, ¶ (C), above, regarding an alleged lack of written description. The claimed method as recited in claims 12 and 13 is not limited in any way to a use in the detection and diagnosis of colon cancer or colon polyps. In fact, no such reference is made to that effect in either claim. The identity of the molecules or compounds that specifically bind the claimed polynucleotides or their mechanisms of interaction need not be disclosed in order to "enable" the skilled artisan to practice the claimed method, only that the method be sufficiently described that the skilled artisan my use it to identify such molecules or compounds. The use of the molecules or compounds so identified is totally at the discretion of the skilled artisan. Withdrawal of the rejection of claims 12 and 13 under 35 U.S.C. § 112, first paragraph, for lack of enablement is therefore requested.

35 U.S.C. § 102(e), Rejection of Claims 1, 2, 4-10, 12 and 13

The Examiner has maintained the rejection of claims 1, 2, 4-10, 12 and 13 under 35 U.S.C. § 102(e) as anticipated by Pierce et al. (U.S. 6,146,849) for the reasons of record. The Examiner reiterated that the claims are drawn, in part, to the complement of an isolated cDNA encoding SEQ ID NO:1 (claim 1), and the complement of an isolated cDNA comprising SEQ ID NO:2, 3 and 5.

The Examiner noted that the specification defines "complement" on page 7, lines 11-13 as nucleic acid molecules which are completely complementary over their full lengths to a cDNA of the sequence listing and which will hybridize to cDNA or mRNA under conditions of high stringency. The Examiner stated that Pierce et al disclose the cDNA clone of HL-13 (SEQ ID NO:5) which encodes (nucleotides 34-1011) an amino acid seqeuence identical to the instant SEQ ID NO:1 with the exception of an arginine residue at position 13. The Examiner stated that the complement of this cDNA would hybridize under stringent conditions to the instant SEQ ID NO:2 because there is only one nucleotide difference out of 975 nucleotides of the coding region. Furthermore, the Examiner stated, the instant SEQ ID NO:3-5 would hybridize to the complement of coding sequence of SEQ ID NO:5 as there were not mismatched nucleotides for

SEQ ID NO:3 and only a single mismatched nucleotide for SEQ ID NO:4 and 5. The Examiner then summarized the disclosures of Pierce et al. with respect claims 5-10, 12 and 13 of the instant invention.

The Examiner stated that the definition states that the nucleic acid which is the complement (of a cDNA of the sequence listing) must be completely complementary over "its" full length, referring to the complementary nucleic acid, not "the cDNA" (of the sequence listing). Thus, the Examiner stated, the claims read on isolated cDNAs comprising nucleic acid sequences which are completely complementary in that said nucleic acids contain no mispairings with the cDNA of SEQ ID NO:2 or the nucleic acid encoding SEQ ID NO:1. The definition in the specification does not exclude complementary sequences which are shorter than SEQ ID NO:2. Further, the Examiner stated, the claims read on cDNA comprising said nucleic acids having this property and therefore do not require that the entire cDNA be completely complementary to SEQ ID NO:2 of the nucleic acids encoding SEQ ID NO:1.

Applicants Response

Claims 1-4 have been amended to recite "the complete complement" of a cDNA encoding SEQ ID NO:1 or of SEQ ID NO:2 therefore clarifying that said complementary sequence must be completely complementary to either the cDNA encoding SEQ ID NO:1 or to SEQ ID NO:2. Pierce et al do not teach a sequence completely complementary to either the cDNA encoding SEQ ID NO:1 or to SEQ ID NO:2, or to SEQ ID NO:4 or 5. Withdrawal of the rejection of claims 1, 2, 4-10, 12 and 13 as anticipated by Pierce et al. is therefore requested.

35 U.S.C. § 102(b), Rejection of Claims 1 and 2

The Examiner has maintained the rejection of claims 1 and 2 under 35 U.S.C. § 102(b) as being anticipated by the New England Biolabs Catalog (1993-1994, page 91) for the reasons of record. The Examiner stated that the specification defines "complement" on page 7 of the specification as a nucleic acid which is completely complementary over its full length and will hybridize to the cDNA or mRNA under conditions of high stringency. The definition therefore does not exclude smaller fragments such as the random hexamers recited in the reference which would be completely complementary across their full lengths to SEQ ID NO:1.

Applicants Response

The amendments to claims 1 and 2 have been discussed above. The random hexamers

described in theNew England Biolabs Catalog do not anticipate a polynucleotide completely complementary to a polynucleotide encoding SEQ ID NO:1 or to SEQ ID NO:2, and withdrawal of the rejection is therefore requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE CORPORATION

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